HHS Public Access

Author manuscript

Cancer Nurs. Author manuscript; available in PMC 2015 March 01.

Published in final edited form as:

Cancer Nurs. 2015 ; 38(2): 111–117. doi:10.1097/NCC.0000000000000143.

Antineoplastic Drug Exposure in an Ambulatory Setting: a Pilot Study

Christopher R. Friese, PhD, RN, AOCN®, FAAN[1], **Cristin McArdle, MPH**[2], **Ting Zhau, PhD**[3], **Duxin Sun, PhD**[3], **Ivan Spasojevic, PhD**[4], **Martha Polovich, PhD, RN, AOCN, ®**[5], and **Marjorie C. McCullagh, PhD, RN, PHCNS-BC, COHN-S**[1]

[1]University of Michigan School of Nursing, Ann Arbor, MI

[2]Michigan State University College of Human Medicine, Department of Epidemiology and Biostatistics, East Lansing, MI

[3]University of Michigan College of Pharmacy, Pharmacokinetics Core, Ann Arbor, MI

[4]Department of Medicine, Duke University Medical Center and Duke Cancer Institute Pharmacokinetics/Pharmacodynamics Bioanalytical Core Lab, Durham, NC

[5]Duke Oncology Network, Durham, NC

Abstract

Background—Exposure to antineoplastic drugs confers health risks to workers, yet little is known about the exposure after a drug spill. Nor has the relationship between exposure and organizational factors such as staffing and work environment been studied.

Objective—To evaluate drug spills prospectively using biological measures and correlate drug spills with organizational factors.

Methods—Prospective questionnaires with 8-hour timed urine samples were collected from nursing and pharmacy personnel who reported a drug spill in one academic health center's infusion center. Urine was collected similarly from workers who did not report a spill. Liquid chromatography tandem mass spectrometry techniques identified detectable drug levels. After the prospective sampling period, workers were surveyed on workloads, practice environment, and safety behaviors.

Results—From 81 eligible individuals, 40 participated in the prospective study and 19 completed retrospective questionnaires. Four spills were reported by 9 personnel as multiple employees were exposed to drug spills. Four participants who reported a spill showed detectable levels of antineoplastic drugs. Four participants who did not report a spill had detectable levels of docetaxel. Compared with respondents who did not report a spill, collegial relations with physicians were significantly poorer for workers who reported spills.

Correspondence To: Christopher R. Friese, RN, PhD, AOCN®, FAAN, University of Michigan School of Nursing, 400 North Ingalls, #4162, Ann Arbor, MI 48109-5482 (cfriese@umich.edu) Telephone: 734-647-4308; Fax: 734-647-2416.

Prior Presentations: None

Disclaimers: Dr. Polovich has received honoraria from ICU Medical and B.D.

Conclusions—The study protocol successfully captured drug spill reports and biological samples. Workers have detectable levels of antineoplastic drugs through both drug spills and environmental contamination.

Introduction

For three decades, researchers have documented the adverse effects of hazardous drug exposure.[1-5] Antineoplastic drugs (ADs) are among the most commonly used hazardous drugs identified as carcinogenic by the International Agency for Research on Cancer (IARC).[6-7] Governmental bodies[8] and professional associations[9-10] have published guidelines on safe handling of ADs, yet guideline adoption is suboptimal.[11] These same guidelines have not determined what drug dosages are correlated with health effects. Instead, the guidelines recommend that preventive measures be taken to reduce exposure risk.[9-10] Research efforts have focused on AD exposure assessment and on process developments to reduce exposure, primarily through closed-system transfer devices and personal protective equipment. AD exposures have been monitored through environmental sampling of surface contamination.[12-15] Prospective biological monitoring from humans has been confined to spot urine samples with limited evidence of uptake.[16] Innovative methods have been developed to determine specific urine concentrations of ADs and drug metabolites. These methods have been validated using highly sensitive liquid chromatography electrospray ionization tandem-mass spectrometry to analyze urine samples.[17] These techniques enable prospective studies to examine drug exposure.

Few published studies have examined the relationship between organizational factors and AD exposure. A 2010 study[18] reported 16.9% of surveyed oncology nurses reported dermal or eye exposure to ADs. Self-reported exposures were significantly more likely to occur with poorer nurse staffing levels and decreased performance of two-nurse chemotherapy dosing verification. In addition to adequate staffing, safety behaviors may play an important role in mitigating risk to employees.

AD exposure remains a prevalent problem in oncology settings, limited data are available on acute exposures (i.e., spills of ADs), and prior studies have focused on surveillance and retrospective data collection. The pilot study reported below studies AD exposure prospectively, includes survey reports and biological measures, and explores organizational factors that may influence acute exposures.

Methods

Our study used prospective questionnaires linked to urine samples followed by a retrospective survey to address three research questions: (1) what is the context in which AD spills occur in ambulatory oncology settings, (2) do workers who report AD spills have detectable drug levels, and (3) what organizational factors are associated with AD spills? The institutional review boards of the principal investigator's institution and the participating facility approved the research protocol and all participants completed written informed consent.

Sample and Setting

Nurses, medical assistants (MA), pharmacists, and pharmacy technicians employed in the ambulatory oncology department at one academic medical center were eligible to participate. These employee groups were selected as they have the most frequent contact with ADs and they process multiple doses throughout a shift. To avoid contamination of biological results, exclusion criteria were current tobacco use and current or past receipt of antineoplastic drugs. Study personnel attended scheduled staff meetings to present protocol information to eligible participants. Incentives of $20 gift cards were provided to all eligible participants without obligation.

The participating institution was a large academic medical center with an average daily volume of 100 adult infusion patients. During the six months of prospective data collection, the pharmacy prepared 19, 284 doses of antineoplastic drugs. Employees completed an annual web-based competency on hazardous drug handling policies. Standard practices included: drug preparation in an immediate use pharmacy with a biological safety cabinet, infusion tubing primed with compatible fluid (as opposed to the hazardous drug), tubing connections secured with a closed-system transfer device, and provision of personal protective equipment and chemotherapy spill kits throughout the workspace. Prior to leaving the pharmacy, personnel wiped each chemotherapy bag with alcohol. The personal protective equipment available included KC500 Purple Nitrile Gloves (with tested impermeability to 27 ADs) and Covidien Kendall™ CT5101 impermeable protective gowns. Nursing staff were instructed to keep drugs in the labeled pharmacy bags until the drug was connected to intravenous tubing. The occupational health department offered medical surveillance to all employees. The institution conducted commercially-available biannual surface swipe testing to evaluate environmental contamination.

Prospective Questionnaire

Prospective data collection occurred over a 6-month period. Participants were instructed to complete a questionnaire when a “spill, drip, drop, or leak of chemotherapy” occurred. The following data were requested: drug name(s), estimated spill volume (in mLs), geographic location of spill, number of employees involved in the spill, dermal or eye contact with the agent, the elements of personal protective equipment worn (gown, gloves, eye protection, respirator), their perceived concern over the spill on a 6-point Likert scale (strongly unconcerned – strongly concerned), and the use of a closed system transfer device. Participants could provide open-text comments about the spill. Study personnel sent participants monthly email reminders to report drug spills. The reminders included a link to the prospective questionnaire. The questionnaire link was also placed on the facility's internal homepage.

Urine Collection and Sampling

We replicated a previously-published protocol for prospective urine collection.[16] All participants provided 8 hours of urine. Because our study focused on assessing exposures after a reported spill, we modified the protocol as follows: after a spill occurred and cleanup activities, patient care needs, and institutional procedures were completed, participants completed the questionnaire described above. Next, participants obtained a urine sampling

kit located in an office several hundred yards from the infusion area. Each kit was housed in 16 quart thermal insulated cooler and contained: written instructions for specimen collection and storage, a single-use 500 mL Nalgene® widemouth container, 6 instant ice packs, 2 castille soap packets, a specimen label, and sharpie pen. Participants labeled the container with their unique study identifier and saved all urine for a total of 8 hours. They began their urine collection 4 hours after drug exposure occurred. This timeframe was selected to optimize the potential amount of drug in the urine and yet avoid the risk of dilution.[16] Participants returned the kit the following day for sample processing.

In addition to the samples collected after a drug spill, we obtained urine samples from 8 participants who were cancer center employees that did not experience a drug spill or participate in spill cleanup on the day of urine collection. These participants also provided 8 hours of urine. The procedures for the latter participants were identical to those described above, but they did not complete questionnaires. Because they experienced no acute drug spill, we standardized urine collection for these participants to begin 4 hours before the end of their shift and for the first 4 hours after the end of their shift, for a total of 8 hours. The analytical laboratories were blinded to specimen sources.

Using single-use disposable personal protective equipment, research staff pooled and aliquotted urine as 5 mL samples, and stored at -70 °C. Drugs of interest were detected by liquid chromatography tandem mass spectrometry (LC-MS/MS) based on multiple reaction monitoring (MRM) for high sensitivity and specificity. To estimate the drug level of the detected compounds using calibration curves, stock solution of each drug was serially diluted to provide calibration standards with a concentration range from 1 pg/mL to 10 ng/mL. The calibration standards were mixed with blank urine samples to mimic the biological matrix. The drug concentration in urine was determined based on the respective calibration curves.

Retrospective Questionnaire

At the end of the 6-month prospective period where spills were reported and urine was collected, all participants were invited to complete a paper questionnaire that examined organizational factors hypothesized to influence exposure. Participants returned questionnaires to a sealed collection bin or mailed them with a postage-paid envelope. Reminder emails were sent monthly to increase response rates.

The following measures were collected: practice environment, workload, safety organizing scale, and years of experience. The practice environment was assessed using the previously-validated Practice Environment Scale of the Nursing Work Index (PES-NWI), modified for ambulatory oncology.[19] Items were modified from the original PES-NWI to reflect ambulatory practice and the use of medical assistants. 23 items across six subscales assess the degree to which employees agree the characteristic is present in their work setting: collegial relations with physicians; participation in practice affairs; foundations for quality care; manager leadership, ability, and support; staffing and resource adequacy, and; medical assistant support. Reported Cronbach alphas exceeded 0.80 for all subscales and satisfactory model fit was achieved with structural equation modeling.[19] Subscales are averaged across a 5-point Likert scale where 1 = strongly disagree and 5 = strongly agree. Workload was

assessed as the number of patients the employee had primary responsibility for on the last shift. The Safety Organizing Scale (SOS)[20] evaluates behaviors that promote safe care delivery. These actions include collecting, analyzing, and disseminating information from errors, and conducting proactive checks to minimize harms. Nine items are scored on a 7-point Likert scale (1= not at all to 7 = to a very great extent). Participants indicated their years of clinical experience.

Data Analysis

Prospective survey data from spill reports were analyzed with descriptive statistics. Results from urine samples were expressed in three terms: (1) below the limit of detection (LOD), (2) exceeds the LOD, and (3) exceeds the lower limit of quantification (LLOQ). The limit of detection (LOD) is the lowest detectable drug concentration at which the signal to noise ratio exceeds 3. The lower limit of quantification (LLOQ) is the most difficult threshold to reach and is the lowest quantifiable concentration above which linear regression can be achieved between concentration and peak areas in mass chromatogram. Results that exceeded the lower limit of quantification are reported as detected drug levels in ng/mL. Results that exceed the limit of detection but do not reach the lower limit of quantification are expressed as the number (%) of samples with detectable levels of drug. Retrospective questionnaire data were analyzes with two-sample t-tests to compare differences between exposed and unexposed workers on organizational factors.

Results

The prospective study had 40 participants who completed informed consent (see Figure 1 for a study flow diagram). During the 6-month study period, four unique drug spill events were reported, nine participants who were present at the time of the spill completed questionnaires, and nine urine specimens were provided after a reported exposure. The reported drugs spilled were etoposide, cisplatin, pemetrexed, and docetaxel, with a range in volume from 5 to 70 mLs. All spills occurred in the patient care area and all involved the use of a closed system transfer device. Three of the 4 spills occurred in the most congested area of the infusion center. During the spill, all respondents wore one pair of gloves, no respondent wore two pairs of gloves, and 29% wore a single-use disposable gown. Sixty percent reported zero or a low level of personal concern about the spill. The mean (SD) number of personnel who responded to each spill was 4.2(1.3). None of these events was reported using the facility's online risk management software.

Participants could describe the spill in their own words. All reported spills involved loose connections between the chemotherapy bag and the intravenous tubing or between the tubing and the vascular access device. One spill involved a patient with cognitive impairment who may not have understood they were connected to an infusion pump. Exposed workers reported assisting in the cleanup of patients and exposed surfaces.

Drug Levels from Obtained Urine Samples

The assays for etoposide, docetaxel, and pemetrexed yielded lower limits of quantification (LLOQ) of 0.02, 0.025, and 0.10 ng/mL, respectively. The limit of detection (LOD) was set

as signal to noise ratio of 3 in mass chromatogram. Due to pre-existing capabilities, pemetrexed and docetaxel assays were performed at one laboratory and etoposide assays were performed at a second laboratory. Because cisplatin cannot be detected directly by using LC-MS/MS electrospray ionization mass spectrometry techniques[21] samples were not analyzed for this compound.

Table 1 shows the results of the LC-MS/MS analyses. Each table row reports the findings from either a worker who was present at the time a specific drug was spilled (labeled by the drug spilled) or a participant who provided urine after completing a shift without a drug spill. Urine from 6 workers who reported etoposide exposure and 2 samples from participants who did not have a spill were analyzed for etoposide. Of the 6 urine samples from workers who reported etoposide exposure, 1 sample exceeded the limit of detection (LOD), but not the lower limit of quantification (LLOQ). The samples from workers without a reported drug spill did not yield detectable levels of etoposide. Of the 3 samples analyzed from workers with exposure to docetaxel, pemetrexed, and cisplatin, all were above the LOD for docetaxel and no samples were above the LOD for pemetrexed. All three of these samples exceeded the LLOQ and were expressed as drug levels: 0.58, 0.10, and 0.03 ng/mL. Four samples from workers who did not report a drug spill were above the LOD for docetaxel, but not above the LLOQ.

Retrospective Survey Findings

At the end of the 6-month period were spills were reported and urine was collected (prospective study phase), 19 of the 40 consented participants (47.5%) completed the retrospective questionnaire. All respondents were nursing personnel; no pharmacy personnel responded. Table 2 evaluates differences between participants who reported and did not report a spill. Compared with workers who did not report a spill, those who reported a spill scored significantly lower on the collegial relations with physicians subscale (4.42 vs. 3.21, respectively, $p = .03$). Compared with non-exposed participants, workers who a spill had lower scores on the remaining practice environment subscales, higher workloads, lower scores on the safety organizing scale, and more years of experience, yet these differences did not reach statistical significance.

The study findings prompted practice changes at the participating institution. The investigators amended the scientific protocol with the approval of the institutional review boards to disclose study results in aggregate to participants. The team met face-to-face with the infusion department staff and institutional leadership, where study results, safe handling procedures, institutional policies, and the availability of medical surveillance were reviewed. After dissemination, staff members have increased their use of double gloves when handling ADs. The institution discontinued the practice of reusing impermeable gowns and changed equipment after staff feedback. Currently, the institution is reviewing policies, procedures, and intravenous tubing and connector selection. Additional quality improvement activities regarding patient assignments, infusion scheduling, and cleaning procedures are underway.

Discussion

In this single-site, practice-based pilot study of antineoplastic drug exposure in the ambulatory oncology setting, 4 spills were reported to the study team, all of which involved a hazardous drug.[7] An important finding of this study showed that a single drug spill exposed multiple workers simultaneously. With the exception of pemetrexed, the drugs reported are used frequently in ambulatory oncology settings. The findings suggest that low, but quantifiable levels of the tested drugs are found in health care workers soon after a spill. Nor is exposure limited exclusively to drug spills. Urine samples from cancer center employees who did not report a drug spill had detectable, but no quantifiable levels of docetaxel. The mostly likely explanation for this finding is contamination of surfaces in the infusion area. The findings from those who did and did not report a drug spill suggests that drug spills pose a greater exposure risk to health care workers than routine environmental exposure. Yet is it important for health care workers to understand that antineoplastic drug exposure occurs in the context of both acute spills and routine drug handling events.

Across a 6-week period with 9,762 drug handling events, Connor and colleagues[16] reported 29 spills or splashes. Over the 6-month study period with 19,284 antineoplastic drugs dispensed, 4 spills were reported by nursing personnel. This suggests a lower spill rate than published previously in a multi-site study where individual personnel were provided with drug handling diaries.[16] There is no standard measurement approach for drug spills. Self-report of drug spills is prone to inherent bias that cannot be overcome without direct, continuous practice observation and/or visual recording. The number of drug spills reported in the study is a low estimate due to underreporting and restriction to consented participants.

Two participants with quantifiable levels of docetaxel reported spills involving drugs other than docetaxel. The facility's latest surface swipe testing report identified docetaxel contamination. During spill cleanup, the participants may have also come in contact with surfaces contaminated with docetaxel. As personal protective equipment use was low by study participants, these workers may have handled docetaxel during their shift without adequate protection. It is unlikely docetaxel was administered concurrently with these agents. The structures and molecular weights of paclitaxel and docetaxel differ enough to eliminate the possibility of errant findings using LC-MS/MS.[22] Pre-existing surface contamination with docetaxel likely explains these findings. Surface swipe test monitoring and thorough cleaning of affected surfaces are necessary to reduce environmental exposure.

The participating facility had devoted significant resources for training, supplies, and medical monitoring. Considering the high frequency of unintentional drug exposure reported previously,[18] the current findings are conservative. This only highlights the need for strategies to reduce exposure through environmental modifications and worker adherence to practice guidelines.

We found modest support for a relationship between organizational factors and AD exposure. Nurses who reported drug spills reported significantly less favorable relationships with physicians. Similar trends were observed across other organizational factors, though no other differences were statistically significant. Collegial nurse-physician relationships may

serve as a proxy for stronger teamwork, which has documented importance on a variety of safety behaviors.[23] It is possible, though untested, that organizational factors must be favorable to assure adequate adherence to recommended guidelines and heightened situational awareness.

Limitations

Despite initial receptivity, pharmacy personnel had low participation rates for unclear reasons. The pharmacy physical location and access restrictions limited the ability of study staff to visit to review study procedures and answer questions. The absence of a pharmacist on the study team and low perceived exposure risk are additional explanations. This study was conducted in one facility with a relatively small sample, which limits the generalizability of findings. The absence of statistically-significant differences in the retrospective survey are likely due to this small sample size and warrant confirmation in a larger, multi-site study. It is likely that non-responders to the retrospective survey have differing perceptions than responders. Finally, our LC-MS/MS procedures were performed at two different labs due to pre-existing capabilities. To increase the reliability of biological measures, we recommend all samples be processed for all antineoplastic drugs by one laboratory, followed by independent confirmation by a second laboratory. Finally, the survey findings would be strengthened by baseline collection of survey measures to examine work environments, workloads, and safety behaviors before drug spills are measured. These limitations are presented alongside one of the few published prospective investigations of antineoplastic drug spills and organizational factors in an ambulatory oncology setting.

Conclusions and Implications

Our findings have important implications for clinicians, practice leaders, and researchers. Detectable levels of drugs are found in both the presence and absence of acute drug spills. This finding suggests increased vigilance by staff is warranted throughout the drug preparation, administration, and disposal process. Drug spills pose a significant threat to workers, and increased efforts are needed to minimize worker exposure through strict adherence to published guidelines. These efforts should include structural (e.g., closed system transfer devices), individual (e.g., personal protective equipment adoption), and behavioral (e.g., heightened situational awareness) approaches.[8-10] The 2013 ASCO/ONS revisions to chemotherapy safety standards discuss necessary safe handling education and instruction.[24] The challenge is how to implement these recommendations and optimize worker protection.

Intravenous tubing connections are a significant contributor to chemotherapy spills. This finding should alert practice managers and clinicians to review products carefully for suitability for hazardous drug preparation and administration. Staff should participate actively in selecting personal protective equipment that balances comfort and safety. Practice leaders must promote a culture of safety and blame-free reporting of spills; incidents should be viewed as learning opportunities. As multiple employees were involved in spills, educational efforts should evolve to practical team-based case study approaches.

Several quality improvement opportunities are available. Practices can design and evaluate initiatives to promote recommended use of personal protective equipment. Audit and feedback programs on drug spills and surface contamination reports can target areas and activities at higher risk. Collaborative efforts can share optimal strategies to protect workers and maintain clinical efficiency.

Finally, prospective research studies that evaluate biological hazardous drug exposure are feasible and yield important insights. Future research efforts should focus on intervention development and evaluation, multi-site studies to compare exposures by organizational factors, and studies that correlate exposure to health outcomes. These approaches will generate the necessary evidence to address a thirty-year old problem.

Acknowledgments

Research Support: Dr. Friese was supported by a Pathway to Independence award from the National Institute of Nursing Research (R00NR010750) and through the University of Michigan Comprehensive Cancer Center Support Grant (P30CA46592). Drs. Friese and McCullagh received pilot funds from the University of Michigan's Education and Research Center for Occupational Safety and Health (T42OH008455).

We thank Thomas Connor, PhD, Research Biologist, Division of Applied Research and Technology, National Institute for Occupational Safety and Health for protocol consultation, Dr. Janean Holden and Susan Kuhnke for specimen storage, and Astrid Fishstrom, MSW, Claire He, and Sarah Reinhardt for research assistance. We also thank the leaders and staff from the participating institution.

References

1. Stellman JM, Aufiero BM, Taub RN. Assessment of potential exposure to antineoplastic agents in the health care setting. Prev Med. 1984; 13(3):245–255. [PubMed: 6494107]
2. Connor TH, McDiarmid MA. Preventing occupational exposures to antineoplastic drugs in health care settings. CA Cancer J Clin. 2006; 56(6):354–365. [PubMed: 17135692]
3. Fransman W, Roeleveld N, Peelen S, et al. Nurses with dermal exposure to antineoplastic drugs: reproductive outcomes. Epidemiol. 2007; 18(1):112–9.
4. Valanis B, Vollmer WM, Steele P. Occupational exposure to antineoplastic agents: self-reported miscarriages and stillbirths among nurses and pharmacists. J Occup Environ Med. 1999; 41(8):632–638. [PubMed: 10457505]
5. Fransman W, Peelen S, Hilhorst S, et al. A pooled analysis to study trends in exposure to antineoplastic drugs among nurses. Ann Occup Hyg. 2007; 51(3):231–239. [PubMed: 17337460]
6. International Agency for Research on Cancer. Agents Classified by the IARC Monographs. 1-106 11/12 update. http://monographs.iarc.fr/ENG/Classification/.
7. Connor, TH.; MacKenzie, BA.; DeBord, DG., et al. NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings 2012. Cincinnati, OH: National Institute for Occupational Safety and Health; 2012.
8. Burroughs, GE.; Connor, TH.; McDiarmid, MA., et al. Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings. Cincinnati, OH: National Institute for Occupational Safety and Health; 2004.
9. Chaffee BW, Armitstead JA, Benjamin BE, et al. Guidelines for the safe handling of hazardous drugs: consensus recommendations. Am J Health Syst Pharm. 2010; 67(18):1545–6. [PubMed: 20811033]
10. Polovich, M. Safe Handling of Hazardous Drugs. 2nd. Pittsburgh, PA: Oncology Nursing Press; 2011.
11. Polovich M, Martin S. Nurses' use of hazardous drug-handling precautions and awareness of national safety guidelines. Oncol Nurs Forum. 2011; 38(6):718–726. [PubMed: 22037334]

12. Turci R, Sottani C, Spagnoli G, et al. Biological and environmental monitoring of hospital personnel exposed to antineoplastic agents: a review of analytical methods. J Chromatogr B Analyt Technol Biomed Life Sci. 2003; 789(2):169–209.
13. Hedmer M, Tinnerberg H, Axmon A, et al. Environmental and biological monitoring of antineoplastic drugs in four workplaces in a Swedish hospital. Int Arch Occup Enrivon Health. 2008; 81(7):899–911.
14. Mader RM, Kokalj A, Kratochvil E, et al. Longitudinal biomonitoring of nurses handling antineoplastic drugs. J Clin Nurs. 2008; 18(2):263–269. [PubMed: 18624785]
15. Mason HJ, Blair S, Sams C, et al. Exposure to antineoplastic drugs in two UK hospital pharmacy units. Ann Occup Hyg. 2005; 49(7):603–610. [PubMed: 15964878]
16. Connor TH, DeBord DG, Pretty JR, et al. Evaluation of antineoplastic drug exposure of health care workers at three university-based US cancer centers. J Occup Environ Med. 2010; 52(10):1019–1027. [PubMed: 20881620]
17. Pretty JR, Connor TH, Spasojevic I, et al. Sampling and mass spectrometric analytical methods for five antineoplastic drugs in the healthcare environment. J Oncol Pharm Pract. 2012; 18(1):23–36. [PubMed: 21183556]
18. Friese CR, Himes-Ferris L, Frasier MN, et al. Structures and processes of care in ambulatory oncology settings and nurse-reported exposure to chemotherapy. BMJ Qual Saf. 2012; 21(9):753–759.
19. Friese CR. Practice environments of nurses employed in ambulatory oncology settings: measure refinement. Oncol Nurs Forum. 2012; 39(2):166–172. [PubMed: 22374490]
20. Vogus TJ, Sutcliffe KM. The Safety Organizing Scale: development and validation of a behavioral measure of safety culture in hospital nursing units. Med Care. 2007; 45(1):46–54. [PubMed: 17279020]
21. Minakata K, Nozawa H, Okamoto N, et al. Determination of platinum derived from cisplatin in human tissues using electrospray ionization mass spectrometry. J Chromatogr B. 2006; 832(2):286–291.
22. Zufía López L, Aldaz Pastor A, Aramendia Beitia JM, et al. Determination of docetaxel and paclitaxel in human plasma by high-performance liquid chromatography: validation and application to clinical pharmacokinetic studies. Ther Drug Monit. 2006; 28(2):199–205. [PubMed: 16628131]
23. Kalisch BJ, Lee KH. The impact of teamwork on missed nursing care. Nurs Outlook. 2010; 58(5):233–241. [PubMed: 20934078]
24. Neuss MN, Polovich M, McNiff K, et al. 2013 Updated American Society of Clinical Oncology/Oncology Nursing Society Chemotherapy Administration Safety Standards Including Standards for the Safe Administration and Management of Oral Chemotherapy. J Oncol Pract. 2013; 9(2s):5s–13s. [PubMed: 23914148]

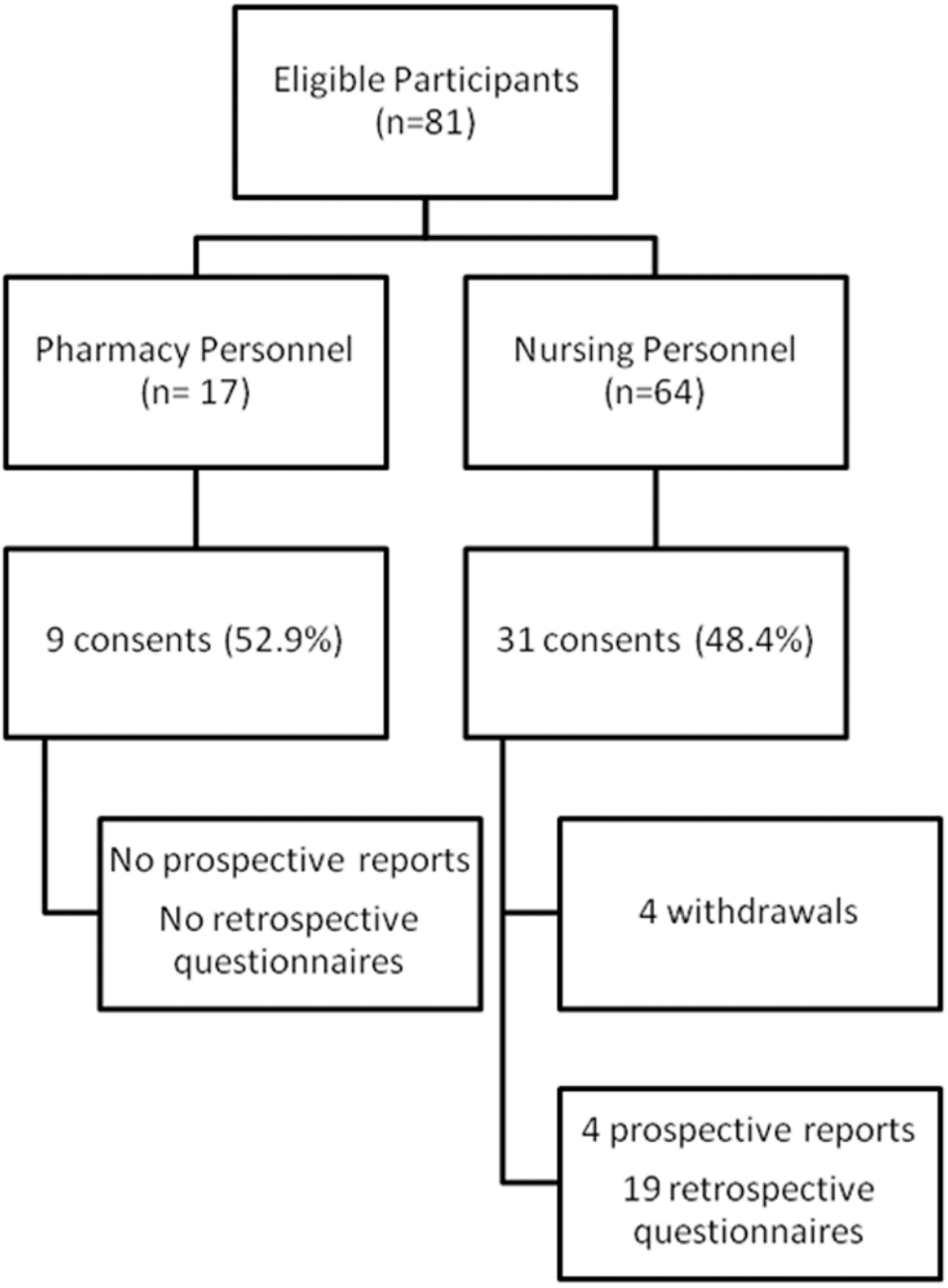

Figure 1.
Study Participant Flow Diagram.

Table 1
Antineoplastic Drug Concentrations Urine Samples

	Etoposide	Docetaxel	Pemetrexed
Lower Limit of Quantification	**0.02 ng/mL**	**0.025 ng/mL**	**0.1 ng/mL**
Sample Analyzed	**Drug Concentration (ng/mL)**		
Reported Etoposide Spill #1	+	N/A	N/A
Reported Etoposide Spill #2	-	N/A	N/A
Reported Etoposide Spill #3	-	N/A	N/A
Reported Etoposide Spill #4	-	N/A	N/A
Reported Etoposide Spill #5	-	N/A	N/A
Reported Etoposide Spill #6	-	N/A	N/A
No Spill Reported Sample #1	-	N/A	N/A
No Spill Reported Sample #2	-	N/A	N/A
Pemetrexed Spill	N/A	**0.58**	-
Docetaxel Spill	N/A	**0.10**	-
Cisplatin Spill	N/A	**0.03**	-
No Spill Reported Sample #3	N/A	+	-
No Spill Reported Sample #4	N/A	+	-
No Spill Reported Sample #5	N/A	+	-
No Spill Reported Sample #6	N/A	+	-
No Spill Reported Sample #7	N/A	-	-
No Spill Reported Sample #8	N/A	-	-

+Sample exceeds level of detection threshold, but is below the lower limit of quantification (LLOQ). Quantitative values in the table represent samples that exceed both level of detection and the lower limit of quantification.

-Below the limit of detection (signal to noise ratio < 3)

N/A: Not analyzed.

Table 2
Organizational Factors and Reported Antineoplastic Drug Exposure (n=19)

Variable	Antineoplastic Drug Spill Reported		*P*
	Yes (n=8)	No (n=11)	
	Mean (SD)		
PES-NWI subscales, revised for ambulatory oncology			
Collegial relations with physicians	3.21 (1.25)	4.42 (0.56)	.03
Participation in practice affairs	4.23 (0.85)	4.69 (0.67)	.20
Manager leadership and ability	4.83 (0.31)	4.91 (0.75)	.74
Foundations for quality of care	4.29 (0.98)	5.44 (0.55)	.14
Supportive relations with medical assistants	4.88 (0.74)	4.45 (1.23)	.38
Number of patients on last shift, personally administered chemotherapy	9.88 (0.34)	8.90 (3.83)	.49
Safety Organizing Scale score	4.81 (1.21)	5.34 (0.70)	.20
Years of experience	18.3 (15.50)	13.7 (9.68)	.41

PES-NWI: Practice Environment Scale of the Nursing Work Index